

# Neuroprotective effects of repeated transient global ischemia and of kynurenine administration induced by four-vessel occlusions on hippocampal CA1 neurons

Jozsef Toldi<sup>1</sup>, Hermina Robotka<sup>1</sup>, Tamas Kopcsanyi<sup>1</sup>, Katalin Sas<sup>2</sup>, Gabriella Rakos<sup>1</sup>, Zsolt Kis<sup>1</sup>, Tamas Farkas<sup>1</sup>, Mate Marosi<sup>1</sup>, Laszlo Vecsei<sup>2</sup>, Eniko Racekova<sup>3</sup> and Jozef Burda<sup>3</sup>

<sup>3</sup>Institute of Neuroscience, Slovak Academy of Sciences, Soltesovej 4, Kosice, Slovak Republic<sup>2</sup>Department of Neurology, University of Szeged, Semmelweis u. 6., Szeged, Hungary<sup>1</sup>Department of Comparative Physiology, University of Szeged, Kozep fasor 52, Szeged, Hungary

The hippocampal CA1 subfield is a brain region that is particularly sensitive to hypoxia. Although this subfield is selectively vulnerable to ischemic injuries manifested in delayed neuronal death (DND), the mechanism leading to neuronal degeneration is not fully understood. Burda recently reported that a second pathophysiological stress, applied within a suitable time, offers an opportunity for salvaging neurons in the CA1 region against DND (Neurochem. Res., 30: 1397-1405, 2005). In our study, NeuN immunohistochemistry was applied to detect survival CA1 neurons, while Fluoro-Jade B staining was used to evaluate the number of injured neurons after interventions resulting in transient global ischemia. Four groups of animals were used: 1: intact controls; 2: sham controls (2 vertebral arteries coagulated (2VAC), but 2 carotids sham-operated); 3: 2VAC + 2 carotids occluded (2CA) for 10 min; 4: 2VAC + 2CA (10 min) + 2 days later, a repeated 2CA (5 min). In group 3 (2VAC + 2CA (10 min)), marked cell destruction was found in the CA1 subfield: only 36.4% of the CA1 neurons survived. However, in group 4 (5-min second ischemic insult), the proportion of surviving cells in the CA1 region was 59.3%. There was no significant difference in CA1 cell loss between groups 1 and 2. Our findings suggest that the second ischemic stress, 2 days after the first ischemia induced by 2VAC + 2CA can be efficient in the prevention of DND. Neuroprotective effect was also found in four-vessel occlusion models after kynurenine (i.v.) administration.

**Acknowledgments:** This project was supported by OTKA (T046687 and M36213), Tét (SK-8/2004), RET-08/04, OMFB-0066/2005 and APVV-51-021904. T. F. is a Bolyai Fellow of the Hungarian Academy of Sciences.